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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/618,350	07/11/2003	John K. Cini	MXI-285	6687

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EXAMINER
LI, RUIXIANG

ART UNIT	PAPER NUMBER
1646	

MAIL DATE	DELIVERY MODE
07/30/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/618,350	CINI ET AL.	
	Examiner	Art Unit	
	RUIXIANG LI	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,9-13,15,17-21,23,25-27,29-31,33 and 35-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-5, 9-13, 15, 17-21, 23, 25-27, 29-31, 33, 35-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

Applicant's amendment filed on 04/15/2008 has been entered. Claims 1, 3-5, 9-13, 15, 17-21, 23, 25-27, 29-31, 33, and 35-39 are pending and under consideration.

Withdrawn Objections and/or Rejections

The rejection of claims 1, 3-5, 9-13, 15, 17-20, 23, 25-27, 29-31, 33, and 35-38 under 35 U.S.C. 112, first paragraph is withdrawn in view of amended claims.

Claim Rejection —35 USC § 112, 1st paragraph

(i). The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(ii). Claims 21 and 39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising an antibody formulated with DTPA and DEF, does not reasonably provide enablement for a pharmaceutical composition comprising an antibody or an antigen-binding fragment thereof formulated with DTPA and DEF. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Applicants argue that an appropriate concentration of DEF can be determined by one of ordinary skill in the art based upon the knowledge available in the art in the prior art and the teachings set forth in Applicants' specification.

Applicants' argument has been fully considered, but is not deemed to be persuasive because the prior art teaches that the acute and chronic toxicity of deferoxamine is relatively high, potentially causing hypotension when administered intravenously (see, e.g., US Patent No. 5,268,165, bottom of column 3). Thus, a composition comprising a high concentration of deferoxamine would not be used by one of skilled in the art for pharmaceutical purposes. However, the claims, as written, *encompass* a composition comprising a high concentration of DEF, which is not suitable for a pharmaceutical purpose. Accordingly, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claim Rejections under 35 USC § 103 (a)

(i). The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

(ii). Claims 1, 3-5, 9, 10, 12, 13, 15, 17-21, 23, 25-27, 29-31, 33, and 35-39 are rejected

under 35 U.S.C. 103(a) as being unpatentable over Foster et al. (US 5,217,954 A, 8 June 1993) in view of Hagiwara et al. (U.S. Patent No. 6,165,467, December 26, 2000), Packer et al. (*Methods in Enzymology*, Volume 186: 41-42, 1990), and Akers (*J. Par. Sci. Tech.* 36:222-228, 1982). The rejection is maintained for the reasons set forth in the previous office action.

Applicants argue that one of ordinary skill in the art would not have been motivated to have combined the teachings of the cited references to arrive at the presently claimed composition. Applicants argue that there was no teaching in the prior art that would have made it predictable that these two agents, in particular, would be especially effective at preventing degradation of an antibody, when combined together. Applicants argue that since Foster et al. and Packer et al. had already discovered that DTPA and DEF in their own right can successfully protect a protein against degradation, one of ordinary skill in the art would have had no reason to combine these two specific agents. Applicants further argue that Applicants' discovery that the unique combination of EGTA and DEF yields a synergistic protective effect was not predictable in view of the teachings of the cited references and, as such, was not prima facie obvious in light of the standard established under KSR.

Applicants' argument has been fully considered, but is not deemed to be persuasive because it would have been obvious to one of skilled in the art to modify the method of Foster et al. to prepare a composition comprising a human monoclonal antibody,

formulated with DTPA and DEF with a reasonable expectation of success. One would have been motivated to do so because Foster et al. teach that the chelators can be used either individually or in combination (bottom of column 1 to top of column 2), Packer et al. teach a chelating agent, desferrioxamine (deferoxamine or DEF), which suppress iron-dependent generation of ·OH from H_2O_2 (2nd paragraph of page 42), and Akers teaches that the use of combination of antioxidant in the same formulation produces a synergistic effect (page 227, the 2nd paragraph). Moreover, a human monoclonal antibody is, in essence, a protein and shares the basic components—amino acids with a protein, including cysteine residues, which are susceptible to oxidation. A human monoclonal antibody possesses characteristics that tend to form aggregates as taught by Hagiwara et al. (the 4th paragraph of column 1). The use of DTPA and DEF would stabilize a composition comprising a human monoclonal antibody.

(iii). Claims 1, 3-5, 9, 10, 12, 13, 15, 17-21, 23, 25-27, 29-31, 33, and 35-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kerwin et al. (US Patent No. 5,929,031, 27 July 1999) in view of Hagiwara et al. (U.S. Patent No. 6,165,467, December 26, 2000), Packer et al. (*Methods in Enzymology*, Volume 186: 41-42, 1990), and Akers (*J. Par. Sci. Tech.* 36:222-228, 1982). The rejection is maintained for the reasons set forth in the previous office action.

Applicants argue that one of ordinary skill in the art would not have been motivated to have combined the teachings of the cited references to arrive at the presently claimed

composition. Applicants argue that there was no teaching in the prior art that would have made it predictable that these two agents, in particular, would be especially effective at preventing degradation of an antibody, when combined together. Applicants argue that since Kerwin et al. and Packer et al. had already discovered that DTPA and DEF in their own right can successfully protect a protein against degradation, one of ordinary skill in the art would have had no reason to combine these two specific agents. Applicants further argue that Applicants' discovery that the unique combination of EGTA and DEF yields a synergistic protective effect was not predictable in view of the teachings of the cited references and, as such, was not prima facie obvious in light of the standard established under KSR.

Applicants' argument has been fully considered, but is not deemed to be persuasive because it would have been obvious to one of skilled in the art to modify the method of Kerwin et al. to prepare a composition comprising a human monoclonal antibody, formulated with DTPA and DEF with a reasonable expectation of success. One would have been motivated to do so because Kerwin et al. teach that one or more of chelators can be used in a formulation (lines 45-51 of column 8), Packer et al. teach a chelating agent, desferrioxamine (deferoxamine or DEF), which suppress iron-dependent generation of $^{\cdot}OH$ from H_2O_2 (2nd paragraph of page 42), and Akers teaches that the use of combination of antioxidant in the same formulation produces a synergistic effect (page 227, the 2nd paragraph). Moreover, a human monoclonal antibody is, in essence, a protein and shares the basic components—amino acids with a protein, including

cysteine residues, which are susceptible to oxidation. A human monoclonal antibody possesses characteristics that tend to form aggregates as taught by Hagiwara et al. (the 4th paragraph of column 1). The use of DTPA and DEF would stabilize a composition comprising a human monoclonal antibody.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.

/Ruixiang Li/
Primary Examiner, Art Unit 1646

Ruixiang Li, Ph.D.
July 28, 2008